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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/807,047 | 06/25/2002 | Jerry Pelletier | Goudreau | 2183 |

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| EXAMINER | |
|---|---|
| LU, FRANK WEI MIN | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1634 | |

DATE MAILED: 07/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/807,047 | PELLETIER ET AL. | |
| | Examiner | Art Unit | |
| | Frank W Lu | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *28 June 2004* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-34,36 and 37* is/are pending in the application.

4a) Of the above claim(s) *20-27 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19, 28-34, and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 April 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ~~4/2001~~.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Election of Species*

1. Applicant's election of species (1) (claims 5-14) and (4) (claims 29 and 30) filed on June 28, 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Therefore, claims 1-19, 28-34, and 37 will be examined.

### *Priority*

2. The examiner notes that applicant has filed a priority document. However, this is no certified copy of Canada patent application 2,246,623 in this instant application, which is required by 35 U.S.C. 119(b).

### *Drawings*

3. The drawings filed on April 6, 2001 appear from applicant's PCT application (PCT/CA99/00933). Each Figure has "SUBSTITUTE SHEET (RULE 26)". Applicant is required to delete "SUBSTITUTE SHEET (RULE 26)" in each Figure in response to this office action.

### *Specification*

4. The disclosure is objected to because of the following informalities: (1) there are several oligonucleotides comprising 10 nucleotides in pages 22 and 25. However, no SEQ ID NO is associated with these oligonucleotides; (2) there are several oligonucleotides comprising 10

nucleotides in Figures 2A, 2D, 3A, 4A, and 5, no SEQ ID NO is associated with these oligonucleotides; and (3) Figures 3A, 4A, and 5 have several oligonucleotides comprising 10 nucleotides. There is no description for these oligonucleotides in BRIEF DESCRIPTION OF THE DRAWINGS.

Appropriate correction is required.

5. Applicant appears to use cover page of PCT/CA99/00933 as an abstract. However, the cover page of PCT/CA99/00933 cannot considered as an abstract. An abstract on a separate sheet is required.

***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 15, 28, and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is referred to the interim guidelines on written description published on December 21, 1999 in the Federal Register at Volume 64, Number 244, pp.71427-71440.

*Vas-Cath Inc. v. Mahurkar,* 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date

sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed". *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

The specification (see page 1, lines 5-15, pages 6-8 and Example 1 in pages 25 and 26) provides adequate written descriptions for a modified oligonucleotide comprising a modification in a homopolymeric sequence that can reduce mispriming between the homopolymeric sequence of the oligonucleotide and its corresponding non-homopolymeric target sequence of a target nucleic acid (or can increase hydrogen bonding between the homopolymeric sequence of the oligonucleotide and its corresponding non-homopolymeric target sequence of a target nucleic acid) and destabilize non-specific duplex formation between the oligonucleotide and the target nucleic acid. However, the specification does not provides adequate written descriptions for a modified oligonucleotide comprising a modification in a homopolymeric sequence that can decrease or abrogate hydrogen bonding between the oligonucleotide and a non-homopolymeric target sequence of a target nucleic acid. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells*

*Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998). Since claims 15, 28, and 37 encompass unknown or unidentified modified oligonucleotides comprising a modification in a homopolymeric sequence that miss from the disclosure, the general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

With limited disclosure provided by the specification, the skilled artisan cannot envision all possible modified oligonucleotides comprising a modification in a homopolymeric sequence recited in claims 15 and 37 and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co.* Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what e has not conceived. See *Fiddes v. Baird,* 30 USPQ2d 1481, 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a modified oligonucleotide comprising a modification in a homopolymeric sequence that can reduce mispriming between the homopolymeric sequence of the oligonucleotide and its corresponding non-homopolymeric target sequence of a target nucleic acid (or can increase hydrogen bonding between the homopolymeric sequence of the oligonucleotide and its corresponding non-homopolymeric target sequence of a target nucleic acid) and destabilize non-specific duplex formation between the oligonucleotide and the target nucleic acid meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant

is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

8. Claims 1-14, 16-19, and 29-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance to show that the modification of a homopolymeric sequence of an oligonuclotide using modified bases in the specification decreases or abrogates hydrogen bonding between said modified oligonucleotide and a non-homopolymeric target sequence. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether modification of a homopolymeric sequence of an oligonuclotide using modified bases in the specification can decrease or abrogate

hydrogen bonding between said modified oligonucleotide and a non-homopolymeric target sequence.

Claims 1-14, 16-19, and 29-34 are directly to a method for destabilizing non-specific duplex formation between a homopolymeric sequence of an oligonucleotide and a non-homopolymeric target nucleic acid comprising a modification of said homopolymeric sequence of said oligonuclotide wherein said modification decreases or abrogates hydrogen bonding between said modified oligonucleotide and a non-homopolymeric target sequence. The specification does not provide a guidance to show that the modification of a homopolymeric sequence of an oligonuclotide using modified bases in the specification decreases or abrogates hydrogen bonding between said modified oligonucleotide and a non-homopolymeric target sequence. In contrast, the specification describes that the modification of a homopolymeric sequence of an oligonuclotide with an universal base reduces mispriming between the homopolymeric sequence and its corresponding non-homopolymeric target sequence of a target nucleic acid and destabilizes non-specific duplex formation between the oligonucleotide and the target nucleic acid (see page 1, lines 5-15, pages 6-8 and Example 1 in pages 25 and 26). This indicates that the modification of a homopolymeric sequence of an oligonuclotide with an universal base increases hydrogen bonding between said modified oligonucleotide and a non-homopolymeric target sequence, which is different from claims 1-14, 16-19, and 29-34. Therefore, in view of the teachings of the specification, it is unpredictable whether the claimed method can be performed and the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether the

modification of a homopolymeric sequence of an oligonuclotide using modified bases in the specification can decrease or abrogate hydrogen bonding between said modified oligonucleotide and a non-homopolymeric target sequence.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-19 and 29-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claim 1 is rejected as vague and indefinite because the goal of the method cannot reach since there is no method step for destabilizing non-specific duplex formation between a homopolymeric sequence of an oligonucleotide and a non-homopolymeric target nucleic acid.

12. Claim 31 is rejected as vague and indefinite because it is unclear what is the relationship between reducing mispriming events from a non-homopolymeric target sequence or maintaining a formation of a duplex with a homopolymeric target sequence and generating *bona fide* genetic markers since reducing mispriming events from a non-homopolymeric target sequence or maintaining a formation of a duplex with a homopolymeric target sequence can not lead generating *bona fide* genetic markers. Please clarify.

13. Claim 32 is rejected as vague and indefinite because it is unclear where an internal A-rich region in an Alu repeat comes from. Does the internal A-rich region in an Alu repeat is from said modified oligonucleotide? Please clarify.

***Conclusion***

14. No claim is allowed.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703)872-9306 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571)272-0782.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
July 14, 2004

FRANK LU
PATENT EXAMINER